Biology of Blood and Marrow Transplantation 14:125-131 (2008)

1083-8791/08/1401-0001$32.00/0
doi:10.1016/j.bbmt.2007.09.016

Acute Renal Failure after Nonmyeloablative Stem Cell Transplantation in Adults

Sabina Kersting, Suzanne V. Dorp, Matthias Theobald, Leo F. Verdonck

Department of Hematology, University Medical Center, Utrecht, The Netherlands

Correspondence and reprint requests: Sabina Kersting, MD, Department of Hematology, B02.226, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands (e-mail: s.kersting@umcutrecht.nl).

Received September 7, 2007; accepted October 17, 2007

ABSTRACT

Acute renal failure (ARF) after myeloablative stem cell transplantation (SCT) is a well-established problem. Little is known about ARF after nonmyeloablative SCT. The aim of the present study was to assess the incidence of ARF and to analyze risk factors for ARF. Moreover, we wanted to study whether ARF influenced survival. We performed a retrospective cohort study of 150 adults who received nonmyeloablative SCT (fludarabine 30 mg/m^2/day for 3 days and/or total-body irradiation (TBI) 200 cGy). ARF was categorized into grade 0 (no ARF), grade 1 (decrease in glomerular filtration rate ≥25% and ≤ doubling in serum creatinine), grade 2 (> doubling in serum creatinine), and grade 2 plus (> tripling in serum creatinine). ARF grade 2-2 plus developed in 49 of 150 patients (33%) after a median of 37 days, 14 patients (9%) had ARF grade 2 plus. No patient required dialysis. Risk factors at baseline for ARF grade 2-2 plus were a history of autologous transplantation ($P = .008$), the absence of vascular disease ($P = .012$) lower serum creatinine ($P < .001$), and higher glomerular filtration rate ($P < .001$). Acute graft-versus-host disease (aGVHD) grade III-IV was the only complication that was associated with ARF ($P = .035$). Overall mortality at 1 year was 23%. Patients with ARF grade 2-2 plus had significantly higher mortality compared to ARF grade 0-1 ($P = .006$). This was largely attributable to a diminished survival in patients with ARF grade 2 plus, who had a mortality rate of 71% caused by, among others, progression of malignancy and GVHD. This makes severe ARF an indicator for decreased survival.

KEY WORDS

Nonmyeloablative stem cell transplantation • Acute renal failure • Acute graft-versus-host disease • Treatment-related mortality

INTRODUCTION

Because treatment-related morbidity and mortality (TRM) limit the success of myeloablative stem cell transplantation (SCT), a nonmyeloablative SCT regimen was developed. This regimen would be suitable for patients of older age and/or comorbidities who were not eligible for myeloablative SCT [1]. Differences between myeloablative and nonmyeloablative conditioning are a reduction in intensities of chemotherapy and of total-body irradiation (TBI) in the nonmyeloablative approach. Because patients' characteristics and transplant procedures are different in the 2 regimens, it is likely that transplant-related organ dysfunction after transplantation will be different also.

Acute renal failure (ARF) after myeloablative SCT is a well-established problem. Incidence ranges from 27%-82%, with need for dialysis in 1%-33% of patients [2-11]. Mortality is increased in patients with ARF, with mortality ranging from 75%-100% in patients who require dialysis [2,3,5,11]. ARF after myeloablative SCT is strongly associated with infectious complications and severe organ dysfunction, for example, hepatotoxicity with jaundice or veno-occlusive disease (sinusoidal occlusion syndrome) [3,4,9,11] sepsis, and use of amphotericin B [9], and mechanical ventilation and admission to intensive care unit [5,9]. Older patients [2,3] and patients with hypertension before transplantation [5] have a higher risk for the development of ARF.

Because patients eligible for nonmyeloablative SCT are usually older and have more comorbid conditions [12], ARF might occur more frequently compared to myeloablative SCT. On the other hand, because of less toxic conditioning regimens and a shorter period

of neutropenia, infectious complications and organ failure will occur less frequently [13], which could have an effect on the incidence of ARF [14].

The aim of the present study was to assess the incidence of ARF and to analyze risk factors for ARF in a large cohort. Moreover, we wanted to study whether ARF influenced survival.

MATERIALS AND METHODS

Patients

Between September 1, 2001, and October 1, 2005, nonmyeloablative SCT was performed in 150 adults aged 20-69 years, at the Department of Hematology of the University Medical Center, Utrecht. Patient data were collected and analyzed retrospectively using a database and patient records through December 1, 2006. Patients gave informed consent and were treated according to clinical protocols approved by the local ethics review board.

The following baseline variables were noted: sex, age, history of autologous transplantation, history of hypertension (defined as a blood pressure $\geq$140/80 mmHg or receiving antihypertensive medication), history of vascular disease (angina pectoris, myocardial infarction, cerebrovascular event, and diabetes mellitus), diagnosis of hematologic disease, malignancy risk (low-risk malignancy: patients with acute leukemia in first complete remission, chronic myelogenous leukemia (CML) in first chronic phase and untreated severe aplastic anemia (AA); high-risk malignancy: all other hematologic diseases), type of transplant (matched related donor, partially matched related donor, matched unrelated donor) and conditioning regimen.

Renal function was assessed according to serum creatinine concentration and estimated glomerular filtration rate (GFR) using the Modification of Diet in Renal Disease equation defined as GFR = $186.3 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ for women})$ [15]. ARF is defined as occurrence of renal dysfunction within 100 days after transplantation and categorized as follows: grade 0 (or normal renal function) is equivalent to a decrease in estimated GFR of <25% of the value at time of transplantation. Grade 1 corresponds to a <2-fold rise in serum creatinine concentration, with a decrease in estimated GFR of >25% of the value at time of transplantation. Grade 2 corresponds to more than doubling in serum creatinine, without indication for dialysis. Grade 2 plus indicates more than tripling in serum creatinine without indication for dialysis. Grade 3 corresponds to ARF requiering dialysis. This classification of grades of ARF is similar to other studies on ARF after stem cell transplantation [9,16,17].

The following variables posttransplantation were registered: acute graft-versus-host disease (aGVHD), cytomegalovirus (CMV) reactivation, admission to intensive care unit, hypertension, and cyclosporine trough levels.

SCT Procedure

The nonmyeloablative conditioning regimen consisted of fludarabine (30 mg/m^2/day for 3 days) followed by TBI of 200 cGy (n = 113) or TBI alone (n = 37). The graft was infused after TBI on day 0. In recipients of a histocompatibility leukocyte antigen (HLA)-matched unrelated donor or a single HLA-antigen mismatched family donor, antithymocyteglobulin (Rabbit ATG, Thymoglobulin™, Genzyme) was given before fludarabine was infused, at a dose of 2 mg/kg/day for 4 days (n = 60). All patients received GVHD prophylaxis orally with cyclosporine and mycophenolate mofetil. Cyclosporine was started on day −3 at 4.5 mg/kg twice daily and continued until day +84 (n = 89) or +120 (n = 61), followed by tapering if no GVHD was present. Dose adjustments were made to keep cyclosporine trough levels between 200 ng/mL and 400 ng/mL. Moreover, the cyclosporine dose was lowered when creatinine rise was caused by cyclosporine, at the discretion of the physician. Mycophenolate mofetil (MMF) was started 5 hours after graft infusion at 15 mg/kg/day, with a maximum dose of 3 g/day until day +28 (n = 89) or +84 (n = 61), followed by tapering if no GVHD was present. GVHD was diagnosed according to the Seattle criteria [18]. aGVHD grade I was treated with topical corticosteroids. aGVHD grade II or higher was treated with high-dose systemic corticosteroids. Infection prevention consisted of ciprofloxacin and fluconazole until granulocyte counts exceeded 500 cell/μL. Cotrimoxazol 480 mg twice daily was given for 15 months, and valacyclovir 500 mg twice daily was given for 12 months.

Statistical Analysis

Continuous variables are displayed as the median, with range in paracentheses. For noncontinuous variables the frequency of occurrence are given along with the corresponding percentage. For comparison of characteristics between groups, a chi-square test was used to compare proportions (or Fisher's exact test where appropriate), and 2-sided Student's *t*-test to compare continuous outcomes.

Those parameters reaching an univariable significance level of $P \leq .1$ were assessed for significance using multiple logistic regressions. Kaplan-Meier survival curves were made for 1 year overall survival (OS). Curves were compared with log-rank test. All *P*-values were 2-sided, and a value of <.05 was considered statistically significant. All analysis was performed using SPSS version 12.0 (SPSS Inc, Chicago IL).

RESULTS

ARF grade 1 (decrease in GFR ≥25% and less than doubling in serum creatinine) developed in 92 of 150 patients (61%) and ARF grade 2-2 plus (more than doubling in serum creatinine, more than tripling in serum creatinine) developed in 49 of 150 patients (33%), with 14 patients (9%) ARF grade 2 plus. None of the patients required dialysis. ARF grade 2-2 plus developed after a median of 37 days (range: 13-91).

Risk factors at baseline for ARF grade 2-2 plus were a history of autologous transplantation (P = .008), the absence of vascular disease (P = .012), lower serum creatinine (P < .001), and higher GFR (P < .001) in univariate analysis (Table 1). In multivariate analysis only the absence of vascular disease and higher GFR were risk factors for ARF (odds ratio [OR] 0.1 95% confidence interval [CI] 0.012-0.790 and OR 1.0 95% CI 1.010-1.042). Sex, age, diagnosis, high-risk malignancy, type of transplant, conditioning regimen, and a history of hypertension did not differ between patients with ARF grade 2-2 plus and patients with grade 0 or 1.

aGVHD grade III-IV was the only complication occurring in the first 100 days that was associated with ARF grade 2-2 plus (P = .035). aGVHD 0-II, the occurrence of hypertension, CMV reactivation, or admission to the intensive care unit was not associated with ARF grade 2-2 plus. Moreover, the immune suppression regimen (cyclosporine +84 and MMF +28 or cyclosporine +120 and mycophenolate mofetil +84) and cyclosporine trough levels (mean of all levels, level at highest creatinine, occurrence of levels ≥400 ng/mL) did not differ between the groups with or without ARF grade 2-2 plus. None of the patients developed thrombotic thrombocytopenic purpura or sinusoidal occlusion syndrome.

ARF in patients with ARF grade 2 plus was caused by: (1) progression of lymphoma in 3 patients, (2) severe diarrhea from GVHD grade III-IV in 5 patients, (3) nephrotoxic medication (ganciclovir and/or cyclosporine) in 4 patients, (4) multiorgan failure on the intensive care unit in 1 patients with sepsis, and (5) dehydration because of pseudomembranous colitis in 1 patient.

Risk factors at baseline for ARF grade 2 plus were higher GFR (P = .045). Complications that were associated with ARF grade 2 plus were aGVHD grade III-IV (P = .014) and CMV reactivation (p = .018). Hypertension occurred significantly less (P = .019) in patients with ARF grade 2 plus. These associations reflect that major causes of ARF grade 2 plus are: severe GVHD with diarrhea and dehydration, which causes hypotension and risk for CMV reactivation because of treatment of GVHD with high-dose prednisolon.

Analysis of patients without ARF (grade 0) showed significantly lower GFR and higher creatinine at baseline, opposite to patients with ARF grade 2-2 plus (data not shown).

Overall mortality at 1 year was 23%. Patients with ARF grade 2-2 plus had a significant higher mortality rate at 1 year (37%) than patients with ARF grade 0-1 (16%) (P = .001 and P = .006) (Table 1). This was largely attributable to a diminished survival in patients with ARF grade 2 plus, who had a mortality rate of 71% at 1 year. Kaplan-Meier survival curves are shown in Figure 1, with a significantly decreased overall survival (OS) in patients with ARF grade 2 plus compared to all other patients (P < .001). There was no significant survival benefit for patients without ARF (grade 0).

There was no significantly difference between treatment related mortality (n = 6) or relapse (n = 4) as cause of death for patients with ARF grade 2 plus. Of the 10 patients with ARF grade 2 plus who died, 3 died of progression of lymphoma that also caused ARF, 4 patients died of GVHD, which also caused ARF, 1 patient died on the intensive care unit of sepsis, which also caused ARF, 1 patient had a sudden death with unknown cause after recovery of ARF because of pseudomembranous colitis, and 1 patient died of relapse of AML after ARF due to cyclosporine. Relapse-related mortality curves and TRM curves are shown in Figures 2 and 3. Patients with ARF grade 2 plus had a significant shorter survival after relapse compared to all other patients (P = .026). There was no significant difference in TRM within 1 year between the patients with the different grades of ARF.

DISCUSSION

In this large single-center cohort of recipients of nonmyeloablative SCT, 33% of patients developed ARF grade 2-2 plus. The incidence of ARF after myeloablative SCT (conditioning with 2 days cyclofosfamide 60 mg/m^2/day and 2 days TBI of 600 cGy/day) was reported as 49% in the same center [5]. More importantly, although 14 patients (9%) developed more than tripling in serum creatinine, none of the patients required dialysis. Parikh et al. [19] found in a multicenter study on nonmyeloablative SCT an incidence of ARF and dialysis of 40% and 4%, respectively, and in a single-center study an incidence of 44% and 3%, respectively [19]. This was lower compared to the myeloablative cohort [20]. In a recent small study of 26 recipients of nonmyeloablative SCT, only 19% developed ARF, with 1 patient requiring dialysis [21]. This indicates that incidence of ARF after nonmyeloablative SCT is lower than after myeloablative SCT. The main reason for lower incidence of ARF is most likely the less toxic conditioning regimen and shorter neutropenia period, which diminishes the incidence of posttransplant complications and infections. In this cohort, no patient developed sinusoidal occlusion syndrome, a complication strongly associated with

Table 1. *Baseline Risk Factors, Complications, and Outcome in Patients with and without ARF*

	All Patients (%)	ARF Grade 2 (%)	ARF Grade 0 and 1 (%)	*P*	Multivariate OR (95%CI)
Sex				ns	
Male	98 (65.3)	29 (59.2)	69 (68.3)		
Female	52 (34.7)	20 (40.8)	32 (31.7)		
Age	56.5 range 20-69	58 range 20-66	56 range 20-69	ns	
History					
Autologous	59 (39.3)	27 (55.1)	32 (31.7)	0.008	
Hypertension	56 (37.3)	19 (38.8)	37 (36.6)	ns	
Vascular disease	17 (11.3)	1 (2.0)	16 (15.8)	.012	0.1 (0.012-0.79)
Diagnosis				ns	
Acute myelogenous leukemia	26 (17.3)	8 (16.3)	18 (17.8)		
Acute lymphoblastic leukemia	5 (3.3)	3 (6.1)	2 (2.0)		
Chronic myelogenous leukemia	5 (3.3)	1 (2.0)	4 (4.0)		
Severe aplastic anemia	6 (4.0)	0 (0)	6 (5.9)		
Multiple myeloma	57 (38.0)	22 (44.9)	35 (34.7)		
Non-Hodgkin lymphoma	25 (16.7)	6 (12.2)	19 (18.8)		
Chronic lymphatic leukemia	10 (6.7)	3 (6.1)	7 (6.0)		
Myelodysplastic syndrome	8 (5.3)	5 (10.2)	3 (3.0)		
Other	8 (5.3)	1 (2.0)	7 (6.9)		
Risk				ns	
High-risk malignancy	123 (82)	41 (83.7)	82 (81.2)		
Low-risk malignancy	27 (18)	8 (16.3)	19 (18.8)		
Type of transplant				ns	
Matched related donor	96 (64.0)	32 (65.3)	64 (63.4)		
Partially matched related donor	8 (5.3)	2 (4.1)	6 (5.9)		
Matched unrelated donor	46 (30.7)	15 (30.6)	31 (30.7)		
Mismatch	21 (14.0)	6 (12.2)	15 (14.9)		
Conditioning				ns	
Fludarabine	1 (0.7)	1 (2)	0 (0)		
Fludarabine/TBI	54 (36)	14 (28.6)	40 (39.6)		
Fludarabine/TBI/ATG	58 (38.7)	17 (34.7)	41 (40.6)		
TBI	37 (24.7)	17 (34.7)	20 (19.8)		
Renal function					
Estimated GFR (mL/min/1.73 m^2)	82 (35-187)	92 (44-187)	78 (35-142)	<.001	1.0 (1.01-1.042)
Creatinine (μmoll/L) median (range)	80 (46-178)	72 (46-123)	85 (57-178)	<.001	
Complications					
Hypertension after transplantation	42 (28.0)	11 (22.4)	31 (30.7)	ns	
CMV reactivation	19 (12.7)	8 (16.3)	11 (10.9)	ns	
ICU admission	6 (4)	3 (6.1)	3 (3)	ns	
aGVHD grade 0-I	80 (53.3)	22 (44.9)	58 (57.4)	ns	
aGVHD grade II	45 (30)	14 (28.6)	31 (30.7)	ns	
aGVHD III-IV	25 (16.7)	13 (26.5)	12 (11.9)	.035	
Cyclosporine trough level >400 ng/L	77 (52)	31 (63.3)	46 (46.5)	ns	
Outcome					
Death at 6 months	23 (15.3)	15 (30.6)	8 (7.9)	.001	
Death at 12 months	34 (22.7)	18 (36.7)	16 (15.8)	.006	
Death from relapse at 12 months	18 (12.0)	8 (16.3)	10 (9.9)	ns	
TRM at 12 months	16 (10.7)	10 (20.4)	6 (5.9)	ns	

TBI indicates total-body irradiation; ATG, antithymocyte globulin; GFR, glomerular filtration rate; CMV, cytomegalovirus; ICU, intensive care unit; aGVHD: acute graft-versus-host disease; TRM, treatment-related mortality; OR, odds ratio; CI, confidence interval; ARF, acute renal failure.
Hypertension: tension >140/90 mmHg.
Vascular disease (angina pectoris, myocardial infarction, cerebrovascular event, and diabetes mellitus).
Low-risk malignancy: patients with acute leukemia in first complete remission, chronic myelogenous leukemia in first chronic phase and untreated severe aplastic anemia. High-risk malignancy: all other hematological diseases.

ARF after SCT following myeloablative conditioning [2-4,11] or mildly reduced intensity conditioning [21].

One of the risk factors for ARF in our study cohort was lower creatinine and a higher estimated GFR at baseline. This is in accordance with previous studies [4,19]. This is most probably affected by the definition of ARF (more than doubling in serum creatinine) used in all the studies on ARF after SCT. The absolute changes required for doubling of serum creatinine is lower for persons with lower creatinine. Patients

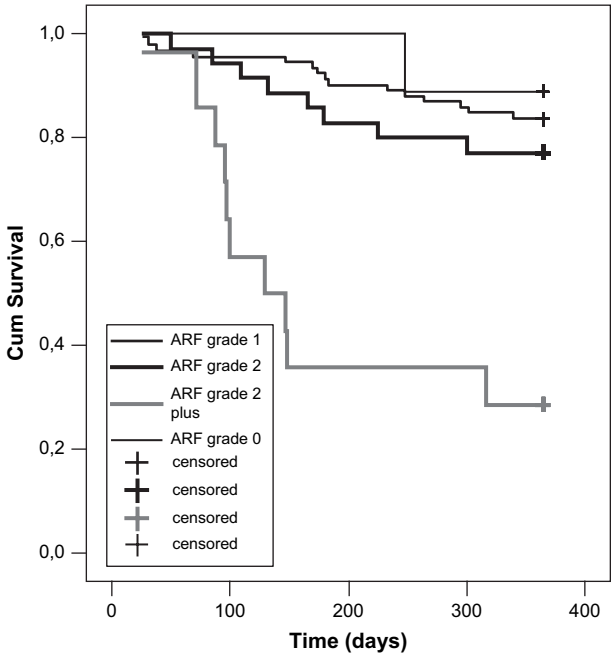

Figure 1. OS curves for the different grades of ARF.

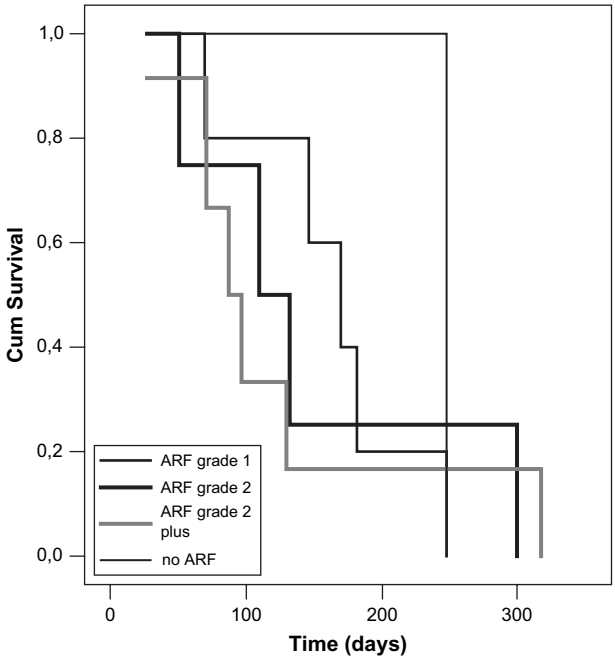

Figure 3. Kaplan-Meier mortality curves for the different grades of ARF in patients with treatment related mortality (TRM) within 1 year (n = 16).

with lower creatinine will therefore meet the definition of ARF grade 2-2 plus sooner. Because serum creatinine is the most important parameter in equations for estimating GFR (both in Modification of Diet in Renal Disease equation and Cockroft and Gault equation), patients with ARF who have lower creatinine at baseline will therefore have higher GFR at baseline. Another explanation for higher incidence of ARF for patients with lower creatinine at baseline may be that the rise in serum creatinine is overlooked because serum creatinine remains in the normal range for healthy individuals.

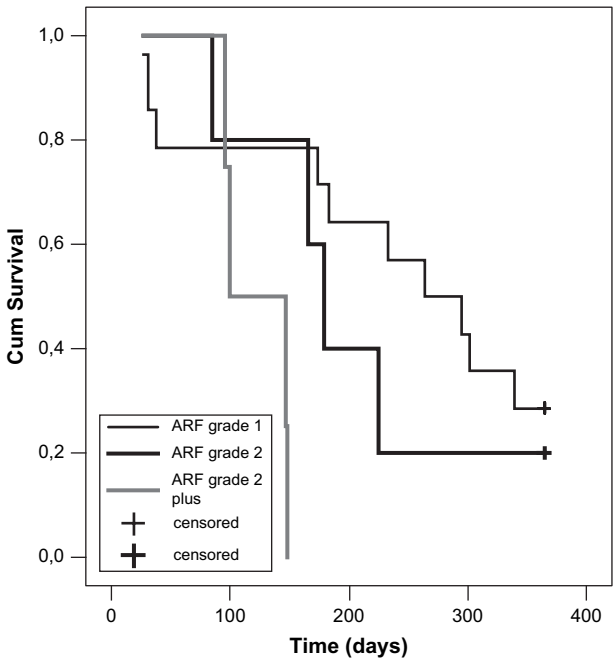

Figure 2. Kaplan-Meier survival curve for the different grades of ARF in patients with relapse of disease within 1 year (n = 23).

Surprisingly, patients with vascular disease had less risk for development of ARF. A possible reason for this is prudence of the physician in monitoring cyclosporine levels and creatinine in this vulnerable patient group. Preexisting diabetes was not associated with ARF in another study [19]. This confirms that nonmyeloablative SCT is suitable for patients with diabetes not eligible for myeloablative transplantation, with regard to renal function.

In our study, neither mean of all cyclosporine trough levels, level at highest creatinine, nor occurrence of levels ≥400 ng/mL corresponded to the development of ARF. This is remarkable, because elevated serum creatinine levels are often ascribed to cyclosporine [1,12]. Although Parikh et al. [19] did not find a correlation between cyclosporine and ARF in univariate analysis, by chart review cyclosporine appeared to be related to grade 2 ARF in almost all cases and ARF resolved with lowering of the dose. Also, in our 14 patients with severe ARF, cyclosporine appeared to be the cause in 3 patients. An explanation for the discrepancy between clinical impression and statistical analysis of the effect of cyclosporine on renal function may be the variability in cyclosporine trough levels within a patient and the transient effect of cyclosporine on renal dysfunction. Also, other studies failed to correlate cyclosporine to ARF [4,5,11,19].

The only complication after SCT associated with ARF was severe aGVHD grade III or IV, which is consistent with another study [3]. However, less severe

aGVHD was not a risk factor for ARF, what is in line with previous studies [4,11,19]. This makes GVHD of the kidneys less likely an explanation for the association of severe aGVHD with ARF. Dehydration because of diarrhea in patients with severe aGVHD is most likely the cause of ARF, which was seen in 5 of our patients with more than tripling of serum creatinine.

In a previous study a risk factor for ARF was hematopoietic stem cells from bone marrow compared to stem cells from peripheral blood [19]. This was, however, not confirmed in another study [20]. Because all our patients received hematopoietic stem cells from peripheral blood, we could not analyze this issue. Female sex and high-risk malignancy were risk factors for ARF in 1 study [20], but not in another [19], and also not in our study, making it questionable whether female sex and high-risk malignancies predispose for ARF.

Mortality at 1 year was more than twice as high in patients with ARF grade 2-2 plus compared to patients with ARF grade 0-1. This was largely attributable to a diminished survival in patients with ARF grade 2 plus, who had a mortality rate of 71%. Parikh et al. [19]. also found significantly higher mortality in patients with ARF after transplantation, but this was largely attributable to ARF that required dialysis. Mortality in patients requiring dialysis after myeloablative transplantation is known to be very high [2,3,5,11]. In our study, survival was decreased in patients with ARF grade 2 plus, despite the fact that none of our patients required dialysis. Almost all ARF grade 2 plus died of conditions that also caused ARF (eg, progression of lymphoma or severe aGVHD). This indicates that ARF grade 2 plus is not the cause of increased mortality, but a strong indicator for decreased survival in patients with ARF secondary to other causes.

Adequate monitoring of serum creatinine remains crucial in detecting drug-induced nephrotoxicity and to stop or adjust the dose of nephrotoxic drugs where possible. Because aGVHD grade III is a major complication associated with ARF, prevention and treatment of severe GVHD is a very important issue in diminishing the occurrence of ARF.

In conclusion, of all patients after nonmyeloablative SCT one-third will develop ARF. About 10% of patients will develop a severe ARF with high mortality caused by relapse, severe GVHD, or other complications. This makes severe ARF an indicator for decreased survival.

ACKNOWLEDGMENTS

We are grateful to M I. Gerrits and J. vd Giessen (Department of Hematology, University Medical Center Utrecht) for providing data.

REFERENCES

1. Niederwieser D, Maris M, Shizuru JA, et al. Low-dose total body irradiation (TBI) and fludarabine followed by hematopoietic cell transplantation (HCT) from HLA-matched or mismatched unrelated donors and postgrafting immunosuppression with cyclosporine and mycophenolate mofetil (MMF) can induce durable complete chimerism and sustained remissions in patients with hematological diseases. *Blood*. 2003;101:1620-1629.
2. Gruss E, Bernis C, Tomas JF, et al. Acute renal failure in patients following bone marrow transplantation: prevalence, risk factors and outcome. *Am J Nephrol*. 1995;15:473-479.
3. Hahn T, Rondeau C, Shaukat A, et al. Acute renal failure requiring dialysis after allogeneic blood and marrow transplantation identifies very poor prognosis patients. *Bone Marrow Transplant*. 2003;32:405-410.
4. Hingorani SR, Guthrie K, Batchelder A, et al. Acute renal failure after myeloablative hematopoietic cell transplant: incidence and risk factors. *Kidney Int*. 2005;67:272-277.
5. Kersting S, Koomans HA, Hene RJ, Verdonck LF. Acute renal failure after allogeneic myeloablative stem cell transplantation: retrospective analysis of incidence, risk factors and survival. *Bone Marrow Transplant*. 2007;39:359-365.
6. Lopes JA, Jorge S, Silva S, et al. Acute renal failure following myeloablative autologous and allogeneic hematopoietic cell transplantation. *Bone Marrow Transplant*. 2006;38:707.
7. Miralbell R, Sancho G, Bieri S, et al. Renal insufficiency in patients with hematologic malignancies undergoing total body irradiation and bone marrow transplantation: a prospective assessment. *Int J Radiat Oncol Biol Phys*. 2004;58:809-816.
8. Nash RA, Antin JH, Karanes C, et al. Phase 3 study comparing methotrexate and tacrolimus with methotrexate and cyclosporine for prophylaxis of acute graft-versus-host disease after marrow transplantation from unrelated donors. *Blood*. 2000;96:2062-2068.
9. Parikh CR, McSweeney PA, Korular D, et al. Renal dysfunction in allogeneic hematopoietic cell transplantation. *Kidney Int*. 2002;62:566-573.
10. Ratanatharathorn V, Nash RA, Przepiorka D, et al. Phase III study comparing methotrexate and tacrolimus (prograf, FK506) with methotrexate and cyclosporine for graft-versus-host disease prophylaxis after HLA-identical sibling bone marrow transplantation. *Blood*. 1998;92:2303-2314.
11. Zager RA, O'Quigley J, Zager BK, et al. Acute renal failure following bone marrow transplantation: a retrospective study of 272 patients. *Am J Kidney Dis*. 1989;13:210-216.
12. McSweeney PA, Niederwieser D, Shizuru JA, et al. Hematopoietic cell transplantation in older patients with hematologic malignancies: replacing high-dose cytotoxic therapy with graft-versus-tumor effects. *Blood*. 2001;97:3390-3400.
13. Maris M, Sandmaier BM, Maloney DG, et al. Non-myeloablative hematopoietic stem cell transplantation. *Transfus Clin Biol*. 2001;8:231-234.
14. Diaconescu R, Flowers CR, Storer B, et al. Morbidity and mortality with nonmyeloablative compared with myeloablative conditioning before hematopoietic cell transplantation from HLA-matched related donors. *Blood*. 2004;104:1550-1558.
15. Manjunath G, Sarnak MJ, Levey AS. Prediction equations to estimate glomerular filtration rate: an update. *Curr Opin Nephrol Hypertens*. 2001;10:785-792.
16. Parikh CR, McSweeney P, Schrier RW. Acute renal failure independently predicts mortality after myeloablative allogeneic hematopoietic cell transplant. *Kidney Int*. 2005;67:1999-2005.

17. Weiss AS, Sandmaier BM, Storer B, Storb R, McSweeney PA, Parikh CR. Chronic kidney disease following non-myeloablative hematopoietic cell transplantation. *Am J Transplant*. 2006;6:89-94.
18. Thomas ED, Storb R, Clift RA, et al. Bone-marrow transplantation (second of two parts). *N Engl J Med*. 1975;292:895-902.
19. Parikh CR, Sandmaier BM, Storb RF, et al. Acute renal failure after nonmyeloablative hematopoietic cell transplantation. *J Am Soc Nephrol*. 2004;15:1868-1876.
20. Parikh CR, Schrier RW, Storer B, et al. Comparison of ARF after myeloablative and nonmyeloablative hematopoietic cell transplantation. *Am J Kidney Dis*. 2005;45: 502-509.
21. Liu H, Ding JH, Liu BC, Zhao G, Chen BA. Early renal injury after nonmyeloablative allogeneic peripheral blood stem cell transplantation in patients with chronic myelocytic leukemia. *Am J Nephrol*. 2007;27:336-341.